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BY

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PROGRESSIVE MUSCULAR DYSTROPHIES:

THE RELATION OF THE PRIMARY FORMS TO ONE ANOTHER AND TO TYPICAL PROGRESSIVE MUSCULAR ATROPHY.*

By B. SACHS, M. D.

THE diseases to be discussed in this article have passed under so many different names that it will be necessary, first of all, to state what shall and what shall not be understood by the term "progressive muscular dystrophies."

This term is intended to designate those forms of disease in which a primary progressive wasting of some or all of the muscles of the body is the most characteristic feature, and in which this wasting (atrophy) may or may not be associated with true or pseudo-hypertrophy of some muscles. These primary progressive dystrophies are our chief concern; we have nothing to do with muscular atrophy following cerebral, myelitic, or peripheral nerve disease. One form of disease, however, which is undoubtedly due to changes in the spinal cord we must draw into the discussion. I refer to typical progressive muscular atrophy. This must, in fact, be the basis upon which our discussion shall proceed, for a very large number of the cases and dif-

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ferent forms of disease which we shall have to consider were once classed under this term. " Progressive muscular atrophy " was for many years, and with many authors still is, a mere clinical designation, just as locomotor ataxia was a mere clinical term until the pathological anatomy of the disease was established, and the term was finally restricted to cases of tabes dorsalis.

Neurologists are at present engaged in sifting the clinical material, and many cases which only a decade ago would have been labeled as " progressive muscular atrophy " are now recognized to be cases of amyotrophic lateral sclerosis, of syringomyelia, of tumor of the cord, of tabes dorsalis, of poliomyelitis anterior infantilis, or of multiple neuritis. I insist again that we have nothing to do with these issues, and that we are concerned with typical progressive muscular atrophy (type Aran-Duchenne) only in its relation to the primary myopathies or muscular dystrophies.

For the purpose of establishing this relation, I propose, with the above limitations in mind, to give a short historical review of our subject. The discussion which is still waging, and which has already succeeded in establishing at least six different forms of progressive muscular wasting, began along two different lines with the creation of two distinct diseases—viz., typical progressive muscular atrophy, and pseudo-hypertrophic muscular paralysis. Let us first take up the history of " progressive muscular atrophy."

Duchenne, in 1849, was the first to describe this disease, and embodied his observations in a paper presented to the French Institute (1). In the next year Aran (2) gave a full description of the same disease and reported a number of cases; the same was done by Cruveilhier (3) three years later, but the full dignity of the disease was not recognized until Duchenne's classic account of it appeared

in his famous work on " L'Électrisation localisée " (4). Duchenne distinguished two forms—progressive muscular atrophy of the adult, and progressive muscular atrophy of infancy. The latter will come up for consideration, together with the new type of muscular atrophy which Landouzy and Déjérine have described and advocated. The former type remains almost in all particulars as Duchenne described it. Modern authors, including Charcot, Leyden, Strümpell, Hammond, Gowers, and others, have been able to add but very little to Duchenne's original description. The chief characteristics of this form are as follows:

Progressive Muscular Atrophy (type Aran-Duchenne). —This form begins in a large majority of the cases with an atrophy and corresponding weakness in the small muscles of the hand (thenar and hypothenar). The atrophy spreads from muscle to muscle ("atrophie individuelle"). Beginning, as a rule, with the adductor pollicis longus, it involves, next in order, the opponens pollicis and deep muscles of the thenar; from these it extends to the hypothenar, the interossei, the flexors and extensors in the forearm. At this stage the disease may remain stationary, or it may spread to the flexors in the upper arm, to the deltoid, possibly the triceps, and finally to the muscles of the trunk, the shoulders, and the back. Duchenne recognized the fact that the atrophy may begin, in exceptional cases, in the trunk, in the shoulders, or in the legs.* Certain it is that in those cases in which the atrophy begins in the

* Of these exceptional cases mentioned by Duchenne a considerable number will now be relegated to other forms of muscular atrophy. Duchenne states that only two cases in one hundred and fifty-nine began in the legs. Hammond said in the first edition of his treatise on "Nervous Diseases," p. 66, .ight cases in twenty-nine; in his last edition, p. 535, he says only six in fifty-two cases.

hands, the legs are not affected until very late in the course of the disease. One marked exception to this rule has occurred in my own practice in the case of a woman aged forty, in whom the atrophy attacked almost simultaneously the small muscles of the thenar and the anterior muscles of the thigh. This case had all the other symptoms of typical progressive muscular atrophy.

The atrophied muscles in progressive muscular atrophy exhibit fibrillar contractions and as a rule retain their faradaic contractility. There may be a diminution of faradaic or galvanic excitability proportionate to the wasting of some muscles, and a complete or partial reaction of degeneration may be present in other muscles. The march of the disease is steadily progressive. Heredity is a strong factor in the disease, as is shown by the remarkable series of cases published by Naunyn and Eichhorst in the "Berliner klinische Wochenschrift," and by the account of the Weathersbee family given in the later editions of Hammond's treatise, although the latter cases probably belong to the peroneal type, to be discussed later on. Osler's cases (5) also give strong proof of heredity.

With the exception of the factor of heredity, all the clinical features, as given above, were known to Duchenne. For many years, too, the clinical features of progressive muscular atrophy were beyond question. All discussions that followed related to the question whether this disease was of spinal or peripheral origin. Duchenne first regarded the disease as of peripheral origin, but in his third edition retracted this view, convinced, as he says, by the pathological and anatomical facts gathered by Charcot and Joffroy (6), Lockhart Clarke (7), Hayem (8), and others (9). To Clarke, and above all to Charcot and his school, we owe the advances made (in the years 1860 to 1870) in our knowledge of the pathology of progressive muscular atrophy.

The main changes found are these : A sclerotic and pigmentary atrophy of the ganglion cells of the anterior horns, inflammatory changes in the neuroglia, increased size of the blood-vessels, and proliferation of the cellular elements. In fresh preparations granular corpuscles are found, and, according to the degree and stage of the disease, the anterior gray cornua are reduced in all diameters, and the ganglion cells either atrophied or entirely lost. The anterior nerve-roots are affected secondarily to the lesion of the gray substance. The nerve-fibers are not all destroyed, a number of them remaining intact. Those that are destroyed exhibit the appearances of simple atrophy—a point to which Charcot * alludes as distinguishing these cases from infantile spinal paralysis.

The theory of the disease was and is, that the inflammation spreads slowly from the ganglion cells of the anterior horns along the anterior nerve-roots without destroying as many of these fibers as is the case in infantile poliomyelitis. The atrophic changes in the muscles are, on this hypothesis, the direct result of the irritation which begins in the cells of the anterior horns and is propagated thence through normal or only half-wasted nerve-roots to the peripheral muscular fiber.

The earlier pathological investigations erred in various respects; first of all, all changes in the spinal cord were not noted, the white columns of the cord were not carefully examined. In consequence of this inadvertence in the examination of pathological specimens and on account of insufficient clinical description, many cases of amyotrophic lateral sclerosis were recorded as cases of progressive muscular atrophy. It is Charcot's great merit to have done pioneer work in this, as in so many other neurological problems. In France, Charcot (10) succeeded in making his

* " Maladies du système nerveux," vol. ii, p. 209.

tephro- (*polio-*) *myélite chronique parenchymateuse* the ana-
tomical substratum of Duchenne's progressive muscular
atrophy.

From this time onward German investigators play a
very important *rôle* in the solution of the problem under
discussion, attacking the problem both from the pathological
and from the clinical standpoint. Bamberger and Reckling-
hausen (11) published two cases of Duchenne's atrophy in
which no changes could be found in the spinal cord post
mortem, but it was not until the appearance of Friedreich's
great monograph (12) that the possible peripheral origin of
progressive muscular atrophy was again pushed into the
foreground.

Friedreich maintained that the changes found in the ante-
rior nerve-roots and in the anterior cornua, in cases of pro-
gressive muscular atrophy, were secondary changes, and to
this he allowed no exception. According to Friedreich's
views, progressive muscular atrophy is a primary chronic
myositis which is followed in due course of time by second-
ary changes in the nervous system. The intermuscular
nerve-filaments are the first to be affected, and from these
nerve-filaments an ascending neuritis travels along the pe-
ripheral nerve-trunk to the anterior roots of the spinal-cord
segment; the neuritis of these anterior nerve-roots may
spread to the cord and here set up chronic myelitic changes
which will vary greatly in degree and distribution; the
extent and character of the changes will, according to
Friedreich, depend upon the extent of the muscular affec-
tion. The changes in the peripheral nerve-fibers and in the
ganglion cells of the anterior horns are the result of the
impaired motor functions of the affected muscles (*op. cit.*, p.
118 and 124).

On this theory alone, Friedreich insisted, can we explain
why in certain cases a wide-spread muscular atrophy is as-

sociated with changes in the cervical segment only, as in the cases of Dumesnil (13), of Lockhart Clarke and Gairdner (14), in the cases of Clarke and Cooper (15), Clarke and Johnson (16), and others, in which changes were found in the spinal cord and none in the nerve-roots. Friedreich claims that the nerve-roots were not properly investigated ; on the other hand, the cases of Recklinghausen, of Friedberg and Cruveilhier, of Trousseau, and his own cases (Nos. 4 and 21), proved to *him* that changes may occur in the muscles themselves, or in the nerve-trunks and anterior nerve roots, and not in the spinal cord ; but Charcot (*op. cit.*, p. 209) very correctly protests that all these cases upon which Friedreich's proof rested were examined before the present successful histological methods for staining the spinal cord had come into vogue, and that they therefore prove nothing.

While Friedreich's judgment unquestionably erred in regard to many of these cases, the error can be explained, since many of the cases upon which he based his views are now known to belong to other forms of muscular atrophy in which there is *no* accompanying change in the spinal cord. As regards typical progressive muscular atrophy, the investigations of later years have put the spinal origin beyond question, although, as Schultze (17) has shown in his excellent monograph, there are but two cases of Duchenne's atrophy [cases of Pierret-Troissier (18) and of Strümpell (19)] in which the anterior gray matter was the *only* part affected, and alone responsible for the wide-spread muscular atrophy. To this list we might add the case of Wood and Dercum (20) if the clinical history were not unsatisfactory. Schultze arrives at his conclusions by excluding even those cases in which the nuclei of the medulla had become involved by extension of the process. Without wishing to depart from the subject before us, I may inti-

mate that these pathological researches prove that, although progressive muscular atrophy is of spinal origin and is a distinct clinical entity, it is not necessarily a morbid entity, and in most cases represents an early stage of one of several spinal-cord diseases.

It is now time for us to retrace our steps and note the development of our knowledge regarding pseudo-hypertrophic muscular paralysis.

The history of this form can be related in few words. The clinical features as laid down by Duchenne, Griesinger, Seidel, and others have been universally accepted. These authors, and all who followed them, fastened upon the increase in the size of some muscles as the characteristic symptom of the disease, and have largely disregarded the wide-spread muscular atrophy which is present in many cases of pseudo-hypertrophy.

The earliest cases of pseudo-hypertrophy of muscles were described by Meryon (21) in 1852. Similar cases had been described by Charles Bell in 1830, but were not valued at their true worth, and Meryon even maintained that his cases were intimately related to Cruveilhier's (Aran-Duchenne's) atrophy. Oppenheim in 1855 published a thesis at Heidelberg on progressive muscular atrophy in which he reported a number of cases of pseudo-hypertrophy, without, however, making a distinction between these cases and Duchenne's type. It was Duchenne again who, in a paper (22) published in 1861, first called attention to the increase in the volume of certain muscles as the important feature in the disease, and in his "Électrisation localisée" established this type of disease for all time. Since that time innumerable cases have been published, enabling Gowers (23) in 1879 to base his studies upon a series of 220 cases, some of these, however, evidently belonging to other categories. The clinical features have been verified so many times over that we

need not in this paper analyze all the cases, but can, without hesitation, present the general features of the disease.

Pseudo-muscular hypertrophy or pseudo-muscular sclerosis (Jaccoud), atrophia musculorum lipomatosa (Seidel) (24), is a disease of early youth, the vast majority of cases beginning before the age of six. Boys are affected somewhat more frequently than girls, and there is good proof of heredity, the disease, although largely affecting boys, being most frequently inherited through the mother. Meryon's cases appeared to form an exception (*vide* Gowers, *op. cit.*, p. 24). The first symptoms are a weakness in the muscles of the leg, a waddling gait, and an apparent increase in the size of some of the muscles of the leg. In many cases the calves only are hypertrophied; in others the calves and thighs, and in rarer cases, like one now under my observation, the disease is limited to, or at least begins in, the thigh muscles.

Author's Case I.—A. K., aged ten. Mother has had six children; one died of "brain fever" and one of croup. Four living, one older than patient, all healthy. No history of heredity. Patient, a stout child, a newsboy, had first teeth at four months; when one year old began to walk. At one year and a half showed weakness and could not walk alone; was provided with some sort of machine with which he learned to walk. Was treated for rickets. Youngest sister has distinct rickets at present. No change until last December, when parents noticed that he was getting lamer. Mother states that thighs were always large; had difficulty in finding trousers that would fit the boy in the thighs. Boy could never walk as other children did, and could never run after others. He now complains of great fatigue, and when walking throws himself down on the grass from mere fatigue. Examination shows increase of volume of anterior thigh muscles of both sides, most marked in the middle portion of the vasti. Calves not hypertrophied; no other atrophy anywhere except in the serratus anticus of the

right side. Grasp of both hands normal; knee-jerks present; all electrical reactions normal. With the assistance of Dr. Peterson I excised two pieces of muscle from the left vastus externus which will be referred to in a later section of this paper. The wound healed readily; boy complains of greater weakness in the leg from which pieces of muscle were removed.

Duchenne made out three stages of the disease. In the first, difficulty in standing and walking, and weakness of muscles of lower extremities and of sacro-lumbar region. In the second stage the hypertrophy becomes the prominent feature, spreading to various muscles of the body, and in the third stage there is increased feebleness of the muscles of upper and lower extremity of the trunk. Other authors recognize a weakening of the sacro-lumbar region and in a general way a weakness of the upper extremities, but, in view of Erb's recent studies, it is due to Gowers to state that he called attention to the fact that in many cases of pseudo-hypertrophy the "infraspinati and deltoids are often increased in size. . . . The latissimus dorsi is commonly much wasted, and so also is the lower (sterno-costal) portion of the pectoralis major. . . . The forearm muscles are rarely affected."

To complete the clinical picture we must in addition refer to the lumbar lordosis (probably due to the weakness of the extensors of the hip), to the occasional presence of contractures, and to the peculiar difficulties in rising from the ground (the patient climbing up upon himself) which are present in some cases, but not necessarily in all, and to which Gowers attaches too much importance in making it the cardinal symptom of the disease. My patient has distinct pseudo-hypertrophy, but rises from the floor with the greatest ease. In a general way it is to be noted that there are no fibrillar contractions in the affected muscles, no changes in the electrical reaction, except diminished excita-

bility to both currents, no sensory disturbances, and the patellar reflex may or may not be present. As a typical example of pseudo-hypertrophy with unusual atrophy of the upper extremities I will cite the following case now under my observation:

Author's Case II.—M. K., girl, aged twelve years and a half; mother has one other child living and healthy. One son died at age of twenty-four of meningitis. Patient first seen by me two years ago. History showed that child had severe fright at age of ten months. Child has always been very nervous; learned to stand and walk at usual age, but had diphtheria at age of four, since when the disease has become much worse. Legs first grew thin. The calves increased in size about four years ago. Child has always had characteristic difficulty in walking and rising from the floor. Examination showed decided weakness in posterior group of leg and thigh muscles; calf and thigh muscles distinctly hypertrophied. Nerves and muscles of lower legs react well to faradaic current, much more readily on indirect than direct excitation. No atrophies anywhere in the body, none around shoulder girdle; hands normal. Child has difficulty in getting upon a chair, and in descending comes down with a bound.

Thigh—left, $13\frac{10}{16}$ inches; right, $13\frac{3}{16}$ inches.

Calves—left, $10\frac{1}{4}$ inches; right, $10\frac{5}{16}$ inches.

Examined the child again after two years; found condition very much the same. Thighs—left side, 16 inches; right, $15\frac{1}{2}$ inches. Calf—left side, 11 inches; right, $10\frac{1}{2}$ inches, showing that the growth of the calf muscles has not kept step with the growth of thigh muscles. Muscles of calf and anterior thigh muscles still appear large. Resistance to passive movements very much diminished, particularly in extensors of thighs. Atrophy of sternal portion of the sterno-cleido-mastoid; left shoulder stands out more prominently than right, but shows no hypertrophy. *All arm and forearm muscles thin;* distinct atrophy in the muscles of the interosseous spaces; grasp very weak; right 18, left 18. In walking, both feet assume valgus position. Arms are in marked contrast to legs. Length of arms, 25 inches;

length of legs, 28 inches.   Electrical examination : All muscles
respond promptly to faradaic current, except interossei and
vasti of both sides, which require very strong currents.   Gal-
vanic response diminished in interossei and in muscles of thenar,
but formula not altered.

Having agreed to accept the foregoing description and
histories as typical of what is ordinarily called pseudo-mus-
cular hypertrophy, we must now devote a little more atten-
tion to the pathological anatomy of the disease.   Cases of
pseudo-hypertrophy with autopsies are relatively few, and
for that reason the evidence must be sifted carefully.

Middleton, in his very excellent paper (25), collected
seventeen cases of pseudo-hypertrophics with autopsies ;
one of these (26) must be excluded from the list as being
a clear case of amyotrophic lateral sclerosis.   Schultze (*op.
cit.*, p. 36) has added to this list the two cases of Middleton,
one by Berger (27), two cases described by Günther (28),
one by Pick (29), and one by Friedreich (*op. cit.*, p. 347),
making twenty-three cases in all.

Of these twenty-three cases, those of Friedreich, Meryon
(Case II), Kesteven (30), Baeg (31), Brigidi (32), Ross (33)
(Case I), and of Günther must be excluded, either because
the spinal cord was not examined microscopically or be-
cause the examination was not properly made.   Of the fif-
teen remaining cases, *the spinal cord and anterior nerve-roots
were found absolutely normal* in ten, and in five others the
changes that were found could not be held responsible for
the changes in the muscles.   These ten cases (34) are un-
objectionable in every point ; their clinical histories are very
similar in every respect and are sufficient proof of the fact
that pseudo-hypertrophy of the muscles is *not* dependent
upon changes in the spinal cord.

In the endeavor to increase this list I have carefully
searched for earlier cases with autopsies, in our own litera-

ture in particular, which might have escaped Schultze's notice, and have furthermore endeavored to collect cases which have appeared since the publication of Schultze's monograph, but the total increase is not great.

First of all, attention should be directed to Gibney's (35) case, which was presented to the American Neurological Association two years ago. The history of the boy, aged sixteen at death, who had been under observation for ten years, is a typical one of the disease. There was first distinct enlargement of the calves, followed later on by atrophy. A brother is affected in the same way. Dr. Amidon, who examined the cord, reports : " The only lesion appeared to be in the ganglion cells of the anterior horns. . . . About one half of the cells seemed to have disappeared, leaving no trace. The remaining ones are poorly defined, small, and in many instances processless. . . . Lesion more marked in the dorsal than in lumbar region."

Through the kindness of Dr. Amidon, I have been permitted to re-examine the specimens, and I must confess that the case would appear to show that there are no serious cord changes in pseudo-hypertrophic paralysis. Processless ganglion cells mean as little in the spinal cord as processless pyramids mean in the cortex, and a diminution in the relative number of cells in any one section is a point exceedingly difficult to determine, and, if present, is more apt to be a secondary than primary affair. I hope that both Dr. Gibney and Dr. Amidon will concur in this view of their case.

The only other cases of pseudo-hypertrophic paralysis *with autopsies* which I have been able to find were these : Westphal (36) reported the cases of two sisters, both affected with typical pseudo-hypertrophy, in the one case characterized by unusual increase in the volume of many muscles and by slight involvement of the facial muscles.

Westphal found *no changes whatever either in the cord or in the peripheral nerves.* Coming from so distinguished an author, these facts deserve the greatest consideration.

Middleton (37) has described another interesting case with enormous pseudo-hypertrophy and a wide-spread atrophy, including even the masseters, but the cord did not harden well and a microscopical examination could not be made. The case is, therefore, useless for our present purposes.

Further autopsies on typical cases of pseudo-hypertrophy are extremely desirable, but Westphal's cases, together with the others analyzed above, place the non-spinal origin of pseudo-hypertrophy beyond question.

These facts do not appear to be properly appreciated as yet, for we find Dr. Inglis (38) very recently reporting several interesting cases of pseudo-hypertrophy and assuming that all pathologico-anatomical facts point to the spinal cord as the seat of disease. Dr. Inglis gets over the discomforting negative facts by stating that " the cases in which the post-mortem examination shows the cord visibly intact do not invalidate this idea (the spinal origin of pseudo-hypertrophy), and that the defect in the distal ends of the motor fibers, while not in every case accompanied by atrophy of the central cells, is yet the indication of an impaired activity of those cells." It is more surprising still to find Hammond (39) disregarding the evidence of the last ten years and adhering to the spinal theory of pseudo-hypertrophic paralysis, and even going so far as to entitle the disease " pseudo-hypertrophic *spinal* paralysis." Hammond's conclusions are based on cases of Barth (40), Müller (41), and Lockhart Clarke (42). Barth's case is one of amyotrophic lateral sclerosis ; Müller's case was complicated by cerebral disease and therefore useless for the determination of the anatomical lesion ; while Lockhart Clarke's case

showed changes which are not primary and which Gowers, whose case this was, acknowledged (in the "Lancet" for 1879) to have been possibly due to the paralysis of long standing and to the frequent pulmonary troubles.

At this stage of our studies let us note that careful clinical investigation and post-mortem examinations have shown among other facts that a wide-spread atrophy is common to progressive muscular atrophy (type Aran-Duchenne) and pseudo-hypertrophy, but that the absence of all changes in the central nervous system, the absence of fibrillar contractions, and the absence of reaction of degeneration in cases of pseudo-hypertrophy, separate it widely from the former disease.   Later on we shall see that a very intimate relation exists, however, between pseudo-hypertrophy and certain other forms of muscular dystrophy which were formerly included under the general heading of progressive muscular atrophy.

The process of distinguishing these forms from progressive muscular atrophy was of slow development, and with the steps of this process we shall become best acquainted by alluding to a few excellent articles published between the years 1870 and 1880.

Lichtheim (43) was one of the first to take up the cudgels for Friedreich's theory of progressive muscular atrophy. In 1878 he published a paper on a case of "progressive muscular atrophy without disease of the ganglion cells of the anterior horns."   A condensed history of his case is as follows :

Louise Groth, aged forty-two.   With exception of an acute fever (typhoid), was well until the age of twenty-seven.   Severe pains in right arm lasting one day and followed next day by weakness in the arm.   Continued her work as laundress for nearly a year in spite of increasing weakness.   Was improved by treatment and resumed her work.   After another year, a

severe confinement (forceps); formation of abscess around right
ankle; right leg grew weaker; weakness and atrophy of right
upper arm were superadded. Worked with interruptions for
seven years longer and gave up work two years and a half pre-
vious to Lichtheim's examination. No hereditary influences.
From the description of loss of function, I infer that the follow-
ing muscles must have been affected: Muscles, wasted—serrati,
right > left; latissimi, right > left; pectorals, right > left;
deltoids, right > left; lower portion of trapezei, right > left;
and various facial muscles (can not pull up nose, frowning dif-
ficult, can close eyes, can not whistle, no difficulty in mastica-
tion or deglutition). Wasted also—intercostals, supraspinati,
biceps brachialis, and supinator longus of both sides; no atro-
phy of forearms or triceps. Thenar and hypothenar wasted,
left > right. Opponens pollicis in fair condition; tremors
when fingers are moved. Gluteal muscles wasted; left calf
slightly larger than the right; no hypertrophy. Abdominal
muscles normal. No sensory disturbances; no reaction of de-
generation; patellar reflex weak but present. Death from phthi-
sis. Autopsy (Cohnheim): *No changes in the cord.* Flexors
of thighs show fatty degeneration; also fatty degeneration and
atrophy of right rectus abdominis. Muscular fibers: atrophy
of contractile elements in diseased muscles; increase of con-
nective tissue, and remaining fibers exhibited a highly nucleated
perimysium internum. No changes in peripheral nerves.

This case of Lichtheim was followed up by one of Erb
and Schultze (44) and one of Kahler (45). The former
authors endeavored to disprove Lichtheim's case by a case
of typical progressive muscular atrophy with changes in the
cord. Erb's criticisms were quite severe, but they have lost
all their force since Schultze showed in later years that
the changes which he and Erb found were not sufficient to
account for the muscular changes, the cells that were atro-
phied being now known to be in no physiological connec-
tion with the muscles that were atrophied; and, further-
more, Erb has since decided that Lichtheim's case, though

a very important one, belongs to the type which Erb (34) first described a few years later. And to this most important class of cases we must now devote our attention.

Erb's Juvenile Form.—Erb described this new form of disease in his " Elektrotherapie," but sufficient attention was not paid to this juvenile form until Erb again described the disease in an article entitled " Ueber die juvenile Form der progr. Muskelatrophie," in the " Dtsch. Arch. f. klin. Med.," 1884.

The following is a typical case of Erb's juvenile form, the history of which will bring out clearly enough the differences of this form and typical progressive muscular atrophy.

Erb's Case I.—Male, aged forty-six. No hereditary history, no syphilis ; several acute diseases in childhood. At the age of fifteen noticed that the right arm was weaker and thinner than the left. No pains or paræsthesiæ. Trouble did not grow worse until about the age of forty ; at that time the legs and left arm became involved ; no sensory, vesical, or sexual disturbances.

Examination revealed changes in the following muscles :

Wasted : Both pectorales major and minor, both trapezii, latissimus dorsi, serrati ant. maj., rhomboids with exception of upper portion of right rhomboid superior, both sacrolumbales and longissimi dorsi, deep neck muscles, levator anguli scapulæ right > left, brachialis anticus right > left, supinator longus (both sides), triceps right > left, gluteal muscles right > left, ilio-psoas right > left, quadriceps, tensor fasciæ ; anterior leg muscles weak with exception of tibialis anticus ; abdominal muscles, diaphragm paretic.

Normal : Sterno-cleido-mastoid, levator anguli scapulæ dexter, coraco-brachialis, flexors and extensors of forearm, thenar and hypothenar, adductors, flexors of leg, calf muscles, small muscles of foot.

Hypertrophied : Deltoid left > right, infraspinati muscles, both teretes.

No ataxia; patellar reflex present ; no fibrillar contractions;

diminished electrical excitability of muscles, but no trace of re-action of degeneration.

The other cases of Erb resembled this one in every respect, except that in at least one of his patients a later examination revealed an incipient hypertrophy of the calves.

Erb has taken the trouble to hunt through medical literature, and proves very conclusively that similar cases have been described by Aran, Duchenne, Friedreich, Ross, and others, either as cases of progressive muscular atrophy or of pseudo-hypertrophy. Erb thus summarizes the chief features of this juvenile form : It is a progressive wasting with weakness of certain groups of muscles, beginning either in childhood or early youth, involving, as a rule, the muscles of the shoulder girdle, the upper arm, the pelvic girdle, the thigh, and the back, the forearm and leg muscles remaining intact for a very long time. The atrophy may be associated with true or pseudo-hypertrophy of some muscles. Fibrillar contractions and reaction of degeneration are never present. No sensory or visceral disturbances. He adds that the wasting is distributed in a typical manner. The pectorals, trapezii, latissimi dorsi, the serrati, the rhomboids, as well as most of the upper arm muscles and supinators, are apt to be wasted, while the deltoids, supraspinati and infraspinati are either normal for a long time or hypertrophied. The preservation, furthermore, of the hand and forearm muscles gives a very striking clinical picture.

This disease Erb has chosen to call the juvenile form of progressive muscular atrophy—a very unfortunate term, since many of the cases exhibited no symptoms until the patient was well advanced in years, and others again began in early infancy. Erb's description has been accepted by Nothnagel, Schultze, Charcot, Eulenburg, Remak, Gowers, and many others.

Upon the exact distribution of the atrophy and hyper-

trophy, as demonstrated by his cases, Erb lays the very greatest stress.   According to his view, well-preserved forearms, atrophied upper arms, hypertrophied deltoids, and wasted scapular muscles would be almost sufficient for a diagnosis of his special form.   In the lower legs an almost analogous change occurs; the thighs and glutæi are well wasted, while the leg muscles and calves are well preserved.

The question arises whether Erb did not attach too much importance to this exact topographical distribution of muscular atrophy and hypertrophy.   He alleges perfect identity between his juvenile form and pseudo-hypertrophy; On page 518 he says : " If this disease occurs in earliest childhood and is not associated with any considerable lipomatosis, the disease is what has been termed hereditary muscular atrophy.   If it happened to be associated with early-developed and excessive lipomatosis, particularly in the lower extremities, it is synonymous with so-called pseudo-hypertrophy. . . . But all of these forms are identical with one another and merely represent different manifestations, a different march of the disease (*Verlaufsweisen*), and varying degrees of intensity of the same disease."

The relation to hereditary muscular atrophy I will discuss later on, but, as for its relationship to pseudo-hypertrophy, is it not curious that Erb's form is so far less frequent than the ordinary pseudo-hypertrophy ?   To be sure, this might be explained in a number of different ways.   First, the accuracy of description has been at fault in many cases.   Most authors have had the hypertrophy, and that only, in mind, and have not, with the exception of Friedreich and Gowers, paid much attention to the atrophy in the upper extremities; and, if detected, most authors have described the atrophy so poorly that a clinical picture such as Erb discovered can not be made out from their descriptions.   This is true not only of older writers, but also of

those that have written since the appearance of Erb's paper.
I have analyzed all recent cases of pseudo-hypertrophy for
the purposes of clinical differentiation, but in the fewest
cases have even the functional motor disturbances been
stated with sufficient clearness to permit an inference as to
the wasting of certain muscles, and definite statements with
regard to the atrophy of this or that muscle are entirely want-
ing in the majority of cases. I wish incidentally to remark
that every case of pseudo-hypertrophy should be examined
with the greatest care regarding the condition of the upper
extremities, and the smallest amount of atrophy or hyper-
trophy of any muscle should be distinctly noted. I have
found a slight change in the faradaic response of symmet-
rical muscles a valuable hint in getting at an incipient wast-
ing with corresponding paresis. Such a condition would,
in at least one case, have escaped my notice if I had not
examined both pectorals and had found that the one gave a
much more lively response to the faradaic current than the
other did.

And yet, allowing for all these possible errors, an ex-
amination of American cases, for instance, has convinced
me that Erb's juvenile form is very much rarer in this coun-
try than typical pseudo-hypertrophy is. In England, Or-
merod (46), Ross (47), and Dreschfeld (48) are the only
ones who have described cases resembling Erb's form, and
Ormerod's case contains several atypical features.* In this
country none have to my knowledge been published as
cases of Erb's juvenile form, though, as Seguin has pointed

* In one of Ormerod's cases there was partial reaction of degenera-
tion in the infraspinatus, the very muscle which Erb found remained
healthy longest; but Ormerod's electrical examinations are not very
satisfactory, for he alludes to the polar formula being altered with re-
gard to the anode—a condition which is found in perfectly healthy
muscles.

out, Mastin's cases of hereditary ataxia may be cases of
Erb's form. I have not been able to get at the original
paper of Mastin. (See Seguin's abstract in " Ann. of the
Univers. Med. Sci.," i, 1888.)

During the past two years I have waited patiently for
an example of Erb's form to turn up, without, however,
meeting with a single one. This disease may be as much
less frequent in America as the Landouzy and Déjérine type
is less frequent in Germany than it is in France. Further-
more, the thought naturally occurs to one that Erb's special
form may represent in many instances a late stage of
pseudo-hypertrophy, and that the majority of cases of this
disease dying at an early age never reach this stage. And
yet we must not forget that Erb has described several cases
of his typical form beginning at a very early age ; and, on
the other hand again, we well know that cases of typical
pseudo-hypertrophy may be associated with atrophy in the
upper extremity without this atrophy assuming Erb's char-
acteristic distribution, as proved by my own case (No. II),
cited above.

In view of such cases as this one and the reasoning fol-
lowed above, it seems to me that the topographical distribu-
tion of the atrophy or hypertrophy can not be depended
upon to prove the absolute identity between pseudo-hyper-
trophy and the juvenile form, and that for the present
pseudo-hypertrophy deserves the rank of a special form.
Their relationship seems to me, however, to rest upon sev-
eral cardinal symptoms which they have in common :

First. Upon a progressive wasting beginning in early
life, associated with hypertrophy at some time during the
course of the disease.

Second. Upon the entire absence of fibrillar contractions.

Third. Upon the absence of the reaction of degenera-
tion.

Fourth. Upon the absence of changes in the spinal cord, the autopsy in Lichtheim's case going to prove this last statement. My friend Dr. Gray ("New York Med. Journal," May 18, 1888) is therefore wrong in stating that no autopsy has ever been obtained in a case of Erb's type.

These cardinal symptoms several other forms of muscular atrophy have in common with the two forms just discussed.

We have now to turn our attention to another type, to the so-called hereditary form of progressive muscular atrophy. This type was created by Leyden (49) and warmly advocated by Möbius (50). According to Leyden, this form is characterized as follows :

The hereditary form of progressive muscular atrophy attacks several members of the same family. It appears at an early age, as a rule between the eighth and tenth years, in one case not before thirty. Males are more apt to be attacked than females (the elder Eulenburg, however, described the affection in three sisters of one family). The disease begins invariably with weakness in the back and lower extremities, and in these regions a wasting of the muscles is first observed. After a lapse of years the muscles of the upper extremities may be involved. Occasionally the patient may attain to an old age. Atrophy may become so extreme that the patients are absolutely helpless. The march of the disease is steadily progressive. Electrical reactions normal; no fibrillar contractions. The atrophy is associated with hypertrophy, particularly of calf muscles. No sensory disturbances, no disturbances of speech, of deglutition, or of ocular movements.

Leyden records the case of a man thirty-seven years of age who had trouble in walking from early childhood on, and who had decided atrophy of back and thigh muscles, with vast increase of calf muscles, without any involvement

of shoulder and arm muscles.   The general symptoms were of the kind stated above.   Leyden counted among this class of cases a well-known one of Meryon (51), the cases of Oppenheimer (52), of Hemptenmacher (53), of Bernhardt (54), and of Eichhorst (55); but all of these cases have been considered by most other and later authors to belong to the type of pseudo-hypertrophy.   Leyden has been followed by Möbius, by Zimmerlin (56), by Landouzy and Déjérine (57), by Schultze (58), and by others in the description of this type; but of these Möbius and the French authors alone can be said to be advocates of this special form.

In my opinion, there is not sufficient reason to create a separate type of disease on the points laid down by Leyden. First, all forms of muscular atrophy may be and often are hereditary.   This is particularly true of pseudo-hypertrophy.   Second, cases with distinct heredity often start in the upper extremities; and third, all cases beginning with weakness and atrophy in the back and leg muscles are not necessarily hereditary, as we shall see when we come to the consideration of my case of the peroneal type of progressive muscular atrophy.

As regards the first point, in the cases of Oppenheim, Friedreich, and Hemptenmacher the disease began in the muscles of the back, but spread to the upper extremities instead of the lower.   Barsikow (59) has described a number of cases occurring in two families.   In the members of the one family the disease attacked back and leg muscles; in the other family the spreading of the atrophy was not uniform, attacking the leg muscles in one member and in another the shoulder first and then the leg muscles.   Zimmerlin (*loc. cit.*) published seven cases—four in one family and three in another.   In the one family the four cases are distinctly of the juvenile type, while in the second family

the two cases began in the upper extremities, leaving the legs intact, while in the third case there was involvement of upper and lower extremities and even involvement of face muscles—an approach to the type Landouzy-Déjérine.

Schultze (*loc. cit.*) describes the cases of two brothers, one affected with typical pseudo-hypertrophy, and the other with a general wasting of the upper and lower extremities. In this country Harrington (59*a*) has reported seven cases in which the onset was in the legs in some, in others in the legs and arms simultaneously, and in still others the legs were affected first, and only a year later the arms.   Ormerod's cases of muscular atrophy in three children after measles might be used to show the same differences in the mode of onset (cf. No. 70).

We have, therefore, good reason for insisting that Leyden's hereditary form is not entitled to rank as a special type of progressive muscular atrophy ; that pseudo-hypertrophy and Erb's juvenile form are distinctly hereditary, and, furthermore, that cases with a distinct heredity are by no means necessarily characterized by an atrophy first attacking the muscles of the back and thighs.   All of Leyden's cases would properly come under the head of pseudo-hypertrophy of Erb's juvenile form, or of the " peroneal type."

The next type of progressive muscular atrophy—the type facio-scapulo-humeral, type Landouzy-Déjérine, the infantile progressive muscular atrophy of Duchenne—can not be disposed of so easily.

Cases of progressive muscular wasting with involvement of face muscles have always been considered rare.   Duchenne described several ; Remak (60), Mossdorf (61), Bernhardt (62), Kreske (63), and Westphal (64) have each described one or two cases, but Landouzy and Déjérine (*loc. cit.*) have succeeded in calling renewed attention to this

form, have made the most careful examinations, and have obtained a post-mortem examination in one case. For this reason it is just to refer to the features of this type as laid down by Landouzy and Déjérine, who have seen more cases than all other recent authors taken together.

The Type Landouzy-Déjérine.—This form of progressive muscular wasting begins, as a rule, in early life, and in the majority of cases in the muscles of the face, giving rise to what the authors term the "*facies myopathique.*" The lips are considerably thickened, and constitute the "*bouche de tapir.*" Great stress is laid upon this tapir-mouth appearance. Later on in the course of the disease the atrophy spreads to the shoulder and arm muscles; the supraspinati and infraspinati, the subscapularis, the flexors of the hand and fingers remain normal. The muscles of deglutition, mastication, and respiratory and laryngeal muscles, as well as the ocular muscles, remain normal. In exceptional cases the disease may begin in the shoulder or arm muscles, or even in the lower extremities. The disease is distinctly hereditary. Fibrillar contractions and reaction of degeneration are never present.

In their first paper Landouzy and Déjérine published cases occurring in two different families; in the first the disease could be followed up through five generations. Cases that are described relate to a father and four sons, five other children not having been affected. The history of one son is characteristic.

The trouble began at the age of three with atrophy of face muscles; no other symptoms observed up to the age of seventeen. From that time on atrophy was noticed in the muscles of the shoulder and arm, spreading to the trunk. At the age of twenty-one atrophy had become extreme—"nothing but skin and bone"—*facies myopathique* and *bouche de tapir.* Sensation normal, sphincters also; patellar reflex lost, electrical excitabil-

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ity diminished in proportion to the wasting, but no reaction of degeneration. At the age of twenty-four, death from phthisis.

Autopsy.—Atrophy determined as follows: Frontalis, orbicularis palpebrarum, zygomatici, orbicularis oris, and buccinator of both sides (levator anguli oris, normal), trapezius, deltoid (infraspinati and supraspinati, subscapularis, teres major and minor, normal), biceps, brachialis anticus, and coraco-brachialis, triceps, supinator longus and extensor radialis (supinator brevis, flexor digitorum sublimis et profundus, normal), extensor pollicis longus and extensor indicis (extensor digitorum communis, extensor digiti minimi, extensor ulnaris, normal), abductor longus and extensor pollicis brevis slightly wasted, abductor brevis pollicis wasted, other thenar and hypothenar muscles normal. Lumbricalis distinctly wasted, and interossei slightly wasted; pectorals wasted; serrati and sacro-lumbar normal. Lower extremities not so carefully examined; glutæi were atrophic; no marked lipomatosis anywhere; no changes in the nervous system. Diseased muscles revealed simple atrophy of primitive muscular fibers; slight traces of increase of interstitial connective tissue and of fat. No increase in muscular nuclei.

The histories of the cases of Remak and of the other authors quoted are very similar. In some the atrophy set in in the extremities first, and in the face later on. In Remak's case both sides of the face were involved; in Kreske's, the one side only.

The similarity between this form and Erb's will be apparent to every one at a glance; it is practically Erb's form plus involvement of face muscles. Erb never observed this complication in his own cases, and Landouzy and Déjérine argue that their cases are different on account of the absence of lipomatosis and the presence of facial symptoms. As for Erb's never having observed the facial atrophy in any of his cases, it is worth noting that in a later paper (65) Landouzy and Déjérine publish a case (No. VI) of their form in which the face muscles appeared normal dur-

ing life, but, on post-mortem examination, revealed decided
morbid changes.   It is possible, therefore, that the same
changes were present in some of Erb's cases without so ex-
cellent an observer as he being able to detect them.   If this
is allowed (and the French authors themselves urge the
possibility of this), there is no just reason for making a
separate type for such cases as they describe.   They deny
the resemblance between the two forms in consequence
also of the invariable absence of lipomatosis; but Westphal
(66) again seems to have found a decisive case which shows
that the face muscles may be associated with typical pseudo-
hypertrophy, and it must be remembered that Landouzy
and Déjérine grant that they have found hypertrophied
fibers in some of the muscles.   We can not, therefore, see
the propriety of creating a separate type such as Landouzy
and Déjérine have described.   There is a slight difference
between their cases and those of Erb in the topographical
distribution of the atrophy, and even this is doubtful, while
their cases resemble Erb's form in the involvement of the
upper arm and shoulder muscles chiefly, in the presence of
hereditary influences, in the absence of fibrillar contractions,
and absence of reaction of degeneration.

I wish, however, to enter a special plea for the recogni-
tion of still another type—the *peroneal type of progressive
muscular atrophy*.   This form was first described by Char-
cot and Marie (67), and, independently of them, by Dr.
Tooth (68), of England, in a Cambridge thesis.   Charcot and
his associate reported five such cases, Tooth four cases, and
Herringham (69) has recently reported one case in a family
in which various members in successive generations have
been similarly affected.   To this list I am able to add one
case of considerable interest; and similar cases, although
not designated by this title, have been described by Ham-
mond (Weathersbee ail), by Ormerod (70), by Schultze (71),

and, no doubt, some other of the cases of hereditary muscular atrophy would more properly belong to this class.

The Peroneal Form of Progressive Muscular Atrophy begins in early youth, or may, as in one of Charcot's cases, attack a person beyond the age of puberty. There may be distinct family inheritance. According to Herringham, as a rule, boys inherit the disease through the mother, as has been shown to be the rule in cases of pseudo-hypertrophy. The atrophy begins in the lower extremities, first attacking the extensor hallucis longus, then the common extensors of the toes, and then the peronei; the small muscles of the foot may be affected as well. The calf muscles atrophy a little later, while the muscles of the thighs offer greater resistance, and do not undergo atrophy until the disease has well run its course. Several years after the onset of the disease in the legs the hands become involved; the interossei, the muscles of the thenar and hypothenar, as well as the muscles of the forearm, become wasted; the supinator longus, the muscles of the shoulder, of the neck, trunk, and face, remain normal. The atrophy need not be entirely symmetrical. Fibrillar contractions occur occasionally; the reaction of degeneration is present in some muscles; the skin reflexes remain normal.

My own case is as follows:

Author's Case III.—R. J., a Russian girl, aged twelve, was referred to my department at the Polyclinic by Dr. Gibney. She is the third child of healthy parents; two born later died—one of diphtheria, and one of cerebral trouble after a fall. No disease similar to the one from which this patient suffers has been known in any branch of the family. While carrying this child, the mother was considerably troubled with swollen feet and legs, possibly of nephritic origin, but is now a healthy, stout woman. The child was asphyxiated when born; no doctor in attendance. Patient began to walk at nine months; had a slight fall at the age of ten months without doing any injury to herself. At the

age of three, mother noticed that there was something wrong with the right knee, and in the hospital in St. Petersburg a plaster-of-Paris splint was put on. This the child wore for seven weeks. She could walk perfectly well after that, and played as well and ran as fast as any child. Has had a number of diseases—measles at the age of one year, small-pox at the age of four, scarlet fever at the age of six, and typhoid fever at six and a half. In spite of all, recovered and walked perfectly well. Came to this country one year ago; nine months ago fell on left hip, and for some weeks had pain in left hip. While recovering from this fall she noticed that she had difficulty in moving the toes of the right leg. This is now five months ago. The impairment of motion gradually grew worse until the child was not able to move the toes at all. Never had pain on her right side. Her present manner of walking developed very slowly. At first sight her gait seemed to be characteristic of poliomyelitis. Child complains of fatigue, particularly in mounting stairs; no other special symptoms. Patient was a bright girl; no hysterical tendencies. The history shows that the present condition of paresis developed slowly, and was not preceded either by convulsions or fever. Furthermore, that there was no pain accompanying the paresis at any time. Has distinct feeling of movement under the skin.

Examination.—Girl of medium size. Upper extremities, good grasp with both hands. Forearm muscles and hand muscles well developed; supinators, also biceps and deltoids, well marked, the latter not hypertrophied. Trapezii and rhomboids of normal strength; right pectoral a little thinner than left. Right shoulder blade shows slight winged appearance. Right serratus slightly weakened. Distinct wasting of the right leg, thigh, and gluteal region. The leg muscles of the right side more distinctly atrophied than the thigh muscles. The child can not lift toes of right foot while resting the heel on the ground. The same movement can be performed fairly well on the left side. Can not raise herself on tip-toes on the right side, but can do so with the left foot. Posterior surfaces of thighs proportionately less developed than anterior surface. Right extensor quadriceps very weak; left weaker

than normal, but stronger than on the right side. Evident
atrophy, therefore, of anterior tibial and posterior tibial group
of right leg, of posterior thigh muscles, and the glutæi muscles
of right side. In the lying position, ten centimetres below
lower edge of the patella, right leg, $23\frac{1}{2}$ ctm.; left leg, $24\frac{1}{2}$ ctm.
Eighteen centimetres below iliac crest, right thigh, 37 ctm.; left
thigh, 39 ctm.

Knee-jerk absent on right side; on left side it was impossi-
ble to obtain the knee-jerk for several weeks; it is now present,
however, and very lively. Occasional fibrillar contractions.
No sensory disturbances anywhere. No rectal or visceral
symptoms. The triceps tendon reflex present on both sides but
weak. Occasional fibrillar contractions have been noticed.

Electrical Examination.—Faradaic examination of all nerves
and muscles gives satisfactory responses except in the case of
the right peroneal nerve, which exhibits diminished faradaic
excitability. On faradaic excitation of peroneal nerve, tibialis
anticus muscle contracts very feebly. Serratus also responds
more powerfully on the left side than on the right to current of
moderate strength. Left pectoralis major does not respond as
well as right to faradaic current. Galvanic examination satis-
factory. The following alone need be mentioned : Examination
with the 10 ctm square electrode : Right peroneal nerve, KCC,
$2\frac{1}{4}$ ma.; AOC, $3\frac{1}{2}$ ma.; ACC, $6\frac{1}{2}$ ma. Left peroneal nerve,
KCC, $2\frac{1}{2}$ ma.; AOC, $3\frac{1}{2}$ ma.; ACC, $6\frac{1}{4}$ ma. Right tibialis
anticus muscle, direct examination, KCC, 7 ma.; ACC, 8 ma.
Left tibialis anticus, KCC, $4\frac{1}{2}$ ma.; ACC, 6 ma. Electrical ex-
amination thus shows a decided diminution of response to the
faradaic current, and to the galvanic current as well in the
tibialis anticus of the right side, the KCC being almost equal to
the ACC. Ormerod would have said that the right peroneal
nerve showed reaction of degeneration with regard to the
anode, but this, I insist, is nothing morbid. We have, there-
fore, slight electrical changes in a single muscle ; the other
muscles of the peroneal group respond normally.

The diagnosis in this case could have rested only be-
tween acute anterior poliomyelitis, a peripheral neuritis, or

this form of progressive muscular atrophy. The mode of
onset, gradually and without pain, without fever or con-
vulsions, argues against a poliomyelitis anterior acuta, as
well as against peripheral neuritis. The atrophy, too, is
not as great as we would expect in a case of spinal infantile
palsy. All of the symptoms—the paralysis proportionate
to the wasting of the muscles, the absence of the knee-
jerk, and the slight changes in electrical reaction—can be
best explained by the diagnosis we have made. Further-
more, the disease is not retrogressive as poliomyelitis acuta
would be, but gradually progressive, and the slight indica-
tions of this progression in the muscles of the trunk lend
further support to the view of a progressive muscular atro-
phy, which is strengthened still more by the occasional
presence of fibrillar contractions.

The diagnosis in such cases as these must be made with
the greatest care, but I have no doubt that some of the
cases which have hastily been put down as cases of periph-
eral neuritis will prove to be cases of this type. From
poliomyelitis anterior acuta it will not be difficult to differen-
tiate this disease, nor from neuritis. It will be more difficult
to distinguish between these cases and those of a wide-
spread atrophy following traumatic joint lesions, in which,
as I have seen a number of times, the atrophy may spread
with surprising rapidity, and may affect the entire ex-
tremity. We must, therefore, either rely upon the history
in these cases, upon the presence or absence of fibrillar
contractions, or must exclude a purely traumatic atrophy in
case the atrophy jumps from the affected part to some
other portion of the body.

In many cases of progressive muscular atrophy of the
typical form the histories show that the disease was first
noticed after some accident. The question therefore arises
whether it may not be possible for typical progressive mus-

cular atrophy to develop after a joint lesion in a subject
predisposed to this disease.

We have now to consider the relations of this peroneal
form of progressive muscular atrophy to the other primary
dystrophies which we have discussed.

It will be seen at once that the anatomical distribution
is entirely different from the four forms of primary myopa-
thies discussed above. If the atrophy spreads to the upper
extremities, it involves the muscles more after the fashion of
a Duchenne's atrophy than after the fashion of a pseudo-
hypertrophy or an Erb's form of atrophy. The analogy to
Duchenne's form becomes still closer when we consider that
this peroneal form is distinguished from the other myopa-
thies by the occasional presence of fibrillar contractions and
by alterations in the reaction of degeneration. The spread-
ing of the atrophy from the muscles of the big toe and the
small muscles of the foot to the muscles of the legs and
thighs reminds one of the manner in which the atrophy
spreads in the upper extremities in cases of typical progres-
sive muscular atrophy. There seems, therefore, to be good
reason to separate this form from the simple muscular my-
opathies and to make it a subdivision of typical progressive
muscular atrophy. This form might be properly entitled
the leg type, in contradistinction to the hand type which
would represent the ordinary form of Duchenne's progres-
sive muscular atrophy.

If the ordinary progressive muscular atrophy is a polio-
myelitis anterior chronica cervicalis, the leg type might rep-
resent a poliomyelitis anterior chronica lumbalis. But this
is speculative pathology and needs corroboration, as indeed
all the clinical and anatomical features of this form do.

In the preceding pages I have given an account of the
commonly received forms of progressive muscular wasting.
Some cases will surely be found that can not properly be

classed under any one of these heads. Schultze's case, for instance, had some of the features of pseudo-hypertrophy, some of those of Erb's form, and in the presence of the fibrillar contractions and reaction of degeneration in some muscles approached to the type of typical progressive muscular atrophy. I have had occasion to observe one case in a child about seven years of age in which there was a general wasting of all the muscles of the body excepting those of the head. The power of the legs and arms was weak, without there being any actual paralysis. There was a winged appearance of the scapulæ, but there were no other disproportionate atrophies or hypertrophies anywhere in the body. The wasting was an entirely uniform one. Such a case as this one is mentioned by Charcot in his recent volume (72) and by Gowers in his text-book. Baeg (*loc. cit.*) and Oppenheim (73) have reported cases with involvement of the face, tongue, laryngeal and ocular muscles, which it is impossible at present to classify under any of the ordinary forms of progressive muscular atrophy.

There is good reason, therefore, for allowing that there are mixed cases of progressive muscular wasting, and that the exact rank of these cases can not be determined at present, except that, according to their cardinal symptoms, they should be classed either with the spinal or primary myopathies.

To complete this study of the various forms of progressive muscular atrophy, it will be necessary to add a few words regarding the histological changes in the muscular tissue. Let me say by way of preface to these remarks that no proper inferences can be drawn from mere harpoon examinations. All such cases I have therefore excluded from the present consideration, and have used with considerable caution even those cases in which pieces of muscle were removed by the knife. As in my own case of pseudo-hyper-

trophy, I believe that very limited inferences only can be drawn from the examination of such small pieces, and that, after all, post-mortem examinations alone are entirely satisfactory in giving evidence regarding all the changes that may occur in the atrophied muscles.

If the histological examination of muscles is to be of value in making a differential diagnosis between the various forms of muscular atrophy, it must help us, first of all, to differentiate between the primary muscular dystrophies and the spinal forms of progressive muscular atrophy.

The changes in muscles atrophied from spinal lesions are: A change in the striation of the fibers and a narrowing of the fibers, an increase in the number of muscle nuclei, and possibly segmentation of the nuclei; granular or fatty degeneration of the fibers, and occasional globules of fat between the muscle-fibrils. I need not add that some or all of these changes will be present according to the length of time the atrophy has existed, and all of these changes have been found both in spinal forms and in primary dystrophies, but the increase in the muscle nuclei is never as great in the latter as in the former form. Furthermore, in the spinal forms hypertrophied fibers are never found, while they are common in the purely muscular types. Müller is the only author who records an exception to this rule, in a case of poliomyelitis of old standing. In spite of this fact, we may say that the presence of any considerable number of hypertrophied fibers, side by side with atrophied and degenerated fibers, is sufficient proof to exclude such a case from the spinal form. Roth (74) professes to be able to differentiate between atrophy from spinal lesion and atrophy following nerve lesion. He states, for instance, that the atrophy of the muscular fibers in progressive muscular atrophy affects the length of a fiber only, causing a shortening, while the breadth of the fiber remains normal. In cases of

muscular atrophy after nerve lesion there is, according to this author, simple atrophy and interstitial sclerosis.

And now the question arises, Is it possible to differenti- ate by histological examination between the various primary myopathies ?   The histological changes of ordinary pseudo- hypertrophy are too well known to need a detailed descrip- tion in this place.   We have, as a rule, narrowing of fibers with changes in their contour, granular or fatty degenera- tion of the fibrils and accumulation of fat globules between the fibrils, and increase without marked proliferation of the connective tissue.   In pieces of muscles excised from the living subject, enlarged fibers will be seen in the immediate vicinity of fibers of normal or less than normal dimensions. In post-mortem examination of muscles in pseudo-hypertro- phy we need not expect to find fibers of unusual breadth, for the examination generally is made at a time when atro- phy has supervened upon a preceding stage of hypertrophy. A slight increase in the muscle nuclei is often found in typ- ical cases of pseudo-hypertrophy, but unusual increase is sus- picious of muscular disease of spinal origin.   It was on the strength of this increase of these nuclei that Friedreich in- sisted that typical progressive muscular atrophy began as a myositis.   Schultze (*loc. cit.*, p. 24) mentions peculiar giant- cell formation as occurring in cases of pseudo-hypertrophy which he regards as the residue of muscular protoplasm with its proliferated nuclei.

Jacoby (75) thinks that the disease consists in the main of a chronic inflammation invading both the perimysium and the muscle tissue, and would call the process a myositis progressiva hyperplastica.   The careful drawings Jacoby has made are very different from the pathological findings in other cases and need further corroboration ; besides, his case is a pseudo-hypertrophy of rather unusual type, exhibit- ing, as the author says, " hypertrophy to an enormous ex-

tent of the deltoids, infraspinati, biceps, triceps, and costal
portion of the pectoralis major." He likens his case to
Case X of Friedreich, and this is now taken to be a case of
Erb's juvenile type. Westphal, in his typical case of pseu-
do-hypertrophy, found, on post-mortem examination, enor-
mous increase of adipose tissue in which the muscular fibrils
were nearly of normal size ; increase of the interstitial con-
nective tissue ; no hypertrophic fibers ; strands of connect-
ive tissue occasionally pass through the fatty tissue, few of
the muscular-fiber groups appearing to be strangulated by
strands of connective tissue.

The sections from the vastus externus of my case of
pseudo-hypertrophy have been cut from tissue hardened in
Müller's fluid and alcohol, and stained with alum-carmin,
hæmatoxylin, and eosin - hæmatoxylin. The specimens
show slight loss of striation, slight increase of connective
tissue and its cells, and a number of enlarged fibers crowd-
ing in upon other and narrower fibers. The changes are
slight in degree, and I have no doubt that if a piece had
been excised from the midst of the muscle, instead of from
its surface, the specimens would have exhibited more de-
cided changes ; but, slight as these changes are, they con-
firm me in the belief that hypertrophy is a very marked
and early change, and is associated with early increase in
the connective tissue.

In Schultze's case, which stands midway between pseudo-
hypertrophy and Erb's juvenile form, the muscles were
examined more exhaustively than ever before. Schultze
found, in addition to the giant-cell formation alluded to
above, large numbers of fat cells in the muscular tissue, an
increase of connective tissue and remnants of hypertro-
phied, normal, and atrophic fibers, and an enormous increase
of nuclei which the author thinks greater than in ordinary
cases of pseudo-hypertrophy, though he quotes one case of

Erb's, of pure pseudo-hypertrophy, in which the finding was entirely similar.   The vacuoles which were present in Schultze's case represent a very late stage in the pathological process, and, if developed to the extent they were in this case, can not be due to hardening.

In Erb's juvenile form most of the conditions are exactly the same, but it is important to note a few points of difference.   In his first paper, in the "Archiv f. klinische Medicin" for 1884, Erb insisted that the hyperplasia and proliferation of the interstitial connective tissue, and next in order the considerable deposit of fat in this connective tissue, were the most characteristic histological features of the disease (p. 492); the atrophy of the fibers and the presence of a few hypertrophic fibers were thought to be features of secondary importance.   In his later articles Erb changes his original opinion and corroborates the hypothesis first put forth by Barsikow—viz., that the hypertrophy of the muscular fibers is the primary and most characteristic change; this hypertrophy may finally pass into an atrophy. Other and secondary features are a rounding off of the contours of the fibers, an increase in the muscle nuclei, an increase of connective tissue and its nuclei, and fissuration and vacuolization of the fibers.   Lipomatosis may occur.

Hitzig (78), the latest author on this subject, has published very careful researches which tend to corroborate Erb's views.   Hitzig has examined four cases; three are typical, one decidedly atypical and suggestive, I think, of amyotrophic lateral sclerosis.   He concludes that "the primary and most important change in juvenile atrophy does not consist of any interstitial process, but is decidedly parenchymatous, and, according to the intensity of the disease, is represented by slight or excessive hypertrophy of the fibers. . . . The anatomical changes in pseudo-hypertrophy, on the other hand, are characterized by active

changes in the connective tissue." If this proves to be correct—and there is a strong probability in its favor—it will corroborate the conclusion I arrived at by an analysis of the clinical facts—that pseudo-hypertrophy and Erb's juvenile form can not be considered entirely identical. Hitzig expresses the opinion also that the atrophy of most fibers is due to mechanical compression by hypertrophied fibers, the hypertrophy being due to an irritative process. The atrophy of the fibers is followed by the deposit of fat, the latter being a mere substitute for the diminished muscular tissue.

In cases that developed most rapidly the atrophy is therefore most extreme. This compression theory of Hitzig will need further corroboration. Singer (79) is in agreement with Hitzig, except that he regards the increase of connective tissue as the first stage in the production of fat.

As to the histological changes in Landouzy and Déjérine's type, we must rely chiefly upon the changes reported in the one case on which Landouzy and Déjérine held an autopsy. They found simple atrophy or entire disappearance of the primitive muscular bundles, a few hypertrophic fibers, but note that the case had taken an exceedingly rapid course. No indication of degenerative atrophy ; very slight increase of interstitial connective tissue and fat, which would seem to prove that the atrophy must be due to some cause within the muscle fibers ; no unusual increase of the nuclei. All this, therefore, is in agreement with Erb's form, and goes to prove the close relationship between these two forms.

The changes in the peroneal form of progressive muscular atrophy have not been reported upon by Charcot and Marie, Tooth, Herringham, or Hoffman (80). In my own case I have not yet obtained permission to excise a piece of

muscle, but hope to do so before long, and it will be interesting to note whether the changes resemble those of primary dystrophies or are similar to those found in muscular atrophy from nerve and spinal lesions. Leyden states that in the hereditary form the muscular changes are the same as in typical progressive muscular atrophy, but his hereditary cases presumably include the peroneal type, and thus his statements might be taken as an indirect histological proof of the close relationship between the peroneal form and typical progressive muscular atrophy.

From this survey of the histological researches in various forms of muscular atrophy we conclude that an examination of muscular changes may help us to differentiate between typical progressive muscular atrophy and the primary myopathies ; and again, if Hitzig is correct, between pseudo-hypertrophy and Erb's juvenile form. There does not, however, appear to be a marked distinction between Erb's juvenile form and the remaining primary dystrophies, the histological changes in the peroneal form being still undetermined.

The argument which has been held throughout these pages leads to the following conclusions :

1. Progressive muscular atrophy, type Aran-Duchenne, is due to spinal-cord disease. The peroneal type of progressive muscular atrophy bears close resemblance to this form and may possibly have a similar pathology.

2. Duchenne's type of progressive muscular atrophy might be termed the hand type, while the peroneal form would represent the leg type.

3. Pseudo-hypertrophy is not of spinal origin. Lipomatosis is a mere incident in the course of the disease and is associated with wide-spread atrophy in various parts of the body.

4. There is a close relationship between pseudo-hyper-

trophy and Erb's juvenile form of progressive muscular atrophy, but not an absolute identity. This close relationship is marked by the onset of the disease at an early age, by the entire absence of fibrillar contractions in both forms, by the absence of reaction of degeneration, and by the occurrence of lipomatosis some time during the course of the disease. They differ from each other in the distribution of the muscular atrophy, and possibly in the histological changes in the affected muscles.

5. Hereditary muscular atrophy does not deserve the rank of a separate clinical entity, all forms of primary myopathies being occasionally hereditary.

6. The type Landouzy and Déjérine is closely related to Erb's form, the additional involvement of the face muscles not being a sufficient basis for a wide clinical differentiation.

7. Pseudo-hypertrophy and Erb's form should be regarded as the two representative forms of primary progressive dystrophies.

8. Primary progressive dystrophies are distinguished from spinal progressive dystrophies by their cardinal symptoms—the onset at an early age, the occurrence of true or false hypertrophy, the absence of the reaction of degeneration, and the absence of fibrillar contractions.

This paper can not be properly closed without reference to the subject of classification. The term " progressive muscular atrophy " has been variously used both to designate the fact of a general and progressive muscular wasting, and also as the proper name for Duchenne's type of atrophy. This has led to great confusion, and it would be well if the term " progressive muscular atrophy " were to be used in a generic sense merely, and if some other name were found for Duchenne's type. Erb's suggestion seems to me to be a good one, and I therefore propose to desig-

nate the type Aran-Duchenne as spinal progressive amyotrophy.

If my argument against the validity of anatomical distribution of atrophies or hypertrophies as a basis for classification be accepted, the classification of muscular atrophies could be reduced to the following simple form:

1. Amyotrophia spinalis progressiva:

    a Hand type;

    β Leg type = peroneal form.

2. Primary progressive dystrophies: *

    a Pseudo-hypertrophy;

    β Erb's form.

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